



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-D-0078]

Principles of Premarket Pathways for Combination Products; Guidance for Industry and Food and Drug Administration Staff; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a final guidance for industry and FDA staff entitled “Principles of Premarket Pathways for Combination Products.” This guidance presents FDA’s current thinking on principles for premarket review of combination products. This guidance includes general, high-level information regarding what combination products are, coordination within FDA and interaction between FDA and sponsors regarding combination product regulation, and how combination products are reviewed by FDA before they are marketed. The guidance also includes recommendations on how to determine which type of premarket submissions may be appropriate for combination products. FDA is publishing this guidance as part of its efforts to implement the 21st Century Cures Act (Cures Act) and in keeping with the Agency’s long-standing commitment to transparency, efficiency, and regulatory consistency to facilitate development of safe and effective combination products. This guidance finalizes the draft guidance of the same title that published on February 6, 2019.

DATES: The announcement of the guidance is published in the *Federal Register* on [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2019-D-0078 for "Principles of Premarket Pathways for Combination Products." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly

viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:

<https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of this guidance to the Office of Combination Products, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 5129,

Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: John Barlow Weiner, Office of Combination Products, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 5129, Silver Spring, MD 20993-0002, 301-796-8930, john.weiner@fda.hhs.gov or combination@fda.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry and FDA staff entitled “Principles of Premarket Pathways for Combination Products.” This guidance presents FDA’s current thinking on principles for premarket review of combination products. This guidance includes general, high-level information regarding what combination products are, coordination within FDA and interaction between FDA and sponsors regarding combination product regulation, and how combination products are reviewed by FDA before they are marketed. The guidance also includes recommendations on how to determine which type of premarket submissions may be appropriate for combination products, as well as illustrative examples.

Section 3038 of the Cures Act (Pub. L. 114–255), enacted in December 2016, substantially amended section 503(g) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353(g)), the principal section of the FD&C Act expressly addressing combination products. General themes of these amendments include enhancing clarity, predictability, efficiency, and consistency of premarket regulatory expectations for combination products, including by ensuring that Agency components and staff coordinate appropriately on premarket review of these products, and that Agency thinking is aligned in conducting these reviews. This guidance is part of FDA’s efforts to implement section 3038 of the Cures Act.

In the *Federal Register* of February 6, 2019 (84 FR 2236), FDA announced the availability of the draft guidance of the same title. FDA received comments and considered those comments as the guidance was finalized. The final guidance clarifies the guidance including its applicability across combination product types and additional detail regarding processes for interacting with the Agency.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on "Principles of Premarket Pathways for Combination Products." It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 3 and in the guidance "How to Prepare a Pre-Request for Designation (Pre-RFD)" have been approved under OMB control number 0910-0523. The collections of information for applications for FDA approval to market a new drug (certain provisions of 21 CFR part 314) have been approved under OMB control number 0910-0001; the collections of information in 21 CFR part 601 have been approved under 0910-0338; and the collections of information in section 351(k) of the Public Health Service Act (42 U.S.C. 262) have been approved under 0910-0719. The collections of information in 21 CFR part 807, subpart E, have been approved under OMB control number 0910-0120; the collections of information in 21 CFR part 814, subparts A through E, have been approved under OMB control number 0910-0231; the collections of information in 21 CFR part 860, subparts A through C, have been approved under OMB control

number 0910-0138; the collections of information in the guidance document “Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program” have been approved under OMB control number 0910-0756; and the collections of information in 21 CFR part 860, subpart D, for De Novo classifications have been approved under OMB control number 0910-0844.

III. Electronic Access

Persons with access to the internet may obtain the guidance at <https://www.fda.gov/combination-products/guidance-regulatory-information/combination-products-guidance-documents>, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>, or <https://www.regulations.gov>.

Dated: January 26, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

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